





UNITED STATES ARMY PUBLIC HEALTH COMMAND (Provisional)

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14. ABSTRACT

Environmental consequences of using specific compounds in military applications have lead to undesirable outcomes. Examples include expensive clean up operations, off-site groundwater migrations, and closing of operational ranges. Additionally, the use of specific weapon systems containing compounds with unknown or limited toxicity data may lead to adverse health consequences to soldiers and civilians. Often incomplete health information has led to inaccurate full life cycle cost estimates. The Army is currently exploring replacement substances for compounds identified as hazardous to health from an environmental and/or occupational (ESOH) perspective. To evaluate the environmental and occupational health consequences of new replacement compounds, a tiered approach has been developed and used within the program. Early in the research stage models are primarily relied upon (e.g. QSAR approaches) and as the technology progresses, a greater reliance is placed on experimental data beginning with in vitro techniques. As greater investment is devoted to system development, less uncertain in vivo data are collected. Together, these data and weighted lines of evidence are used to help guide life cycle decisions in the development of new systems. Examples will be provided.

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# ASSESSMENT OF ENVIRONMENTAL AND OCCUPATIONAL HEALTH IMPACTS IN MUNITIONS AND WEAPON SYSTEMS DEVELOPMENT: A PHASED APPROACH

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# Introduction

- Military Operations require:
  - Unique substances (energetics, explosives, detonators, propellants, etc.).
- Encroachment and health concerns affect readiness and can cost billions.
  - Closing of ranges
  - Cleanup costs
  - NRDA
  - BRAC delays
- Halt/delay/cost new systems/programs
  - Health effects to soldiers
  - Adverse environmental effects
    - Effects to humans and the environment









# Required Documentation (Soldier Health)

- Health Hazard Assessments
  - AR 40-10 HHA Program
  - AR 40-5 Preventive medicine
  - AR 602-2 Army Manprint
  - AR 70-1 Acquisition
- Toxicity Clearances
  - AR 40-5

- AR 70-1

The Army toxicity clearance process supports the PM by providing approval and guidance for the safe use of new materials and chemicals. The PM is responsible for identifying technically feasible materials proposed for a specific Army use and requesting a toxicity clearance through the method delineated in DA Pam 70–3. The U.S Army Public Health Command (prov) is then responsible for developing the toxicity clearance to include approval/disapproval for specific use as well as any safety requirements.





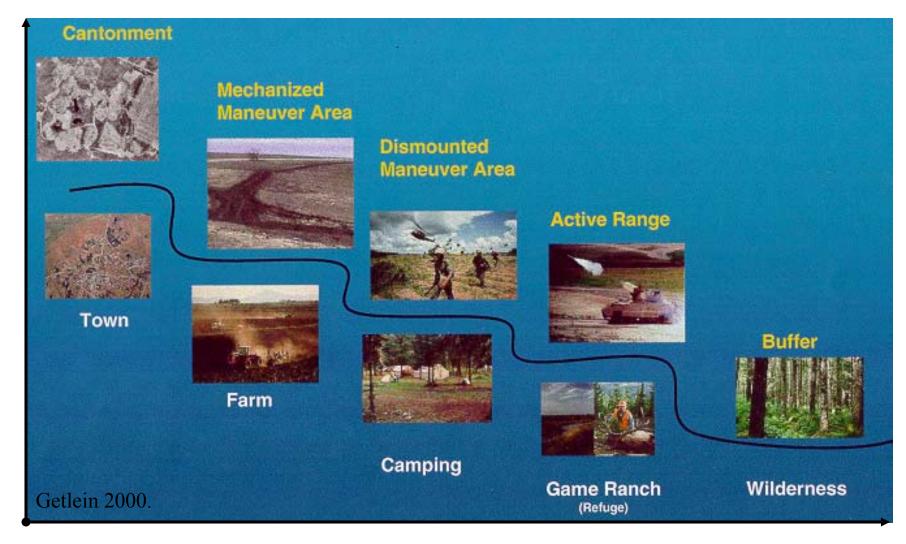
#### **Environmental Health**

- Programmatic Environmental Safety and Health Evaluation (PESHE)
- NEPA
- No data requirement
- No guidance for RDT&E
- Some data are available
- Studies could be harmonized with those for Occupational health
- Utilizes high throughput assays/screens







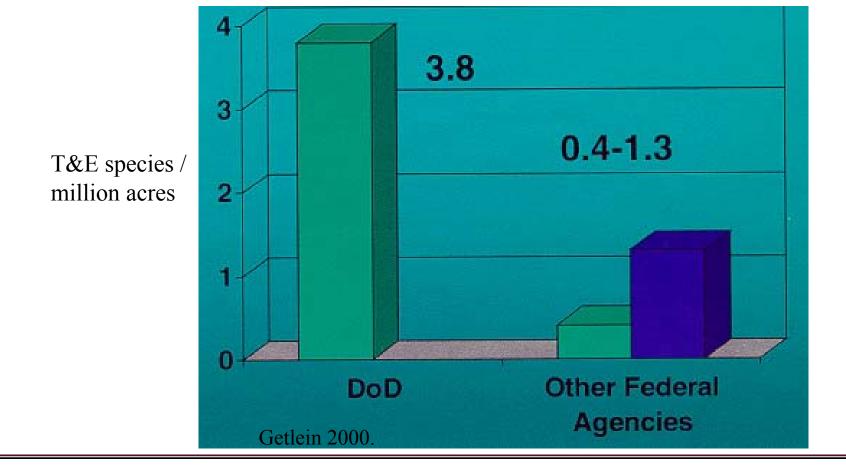


**Increasing Species Richness** 





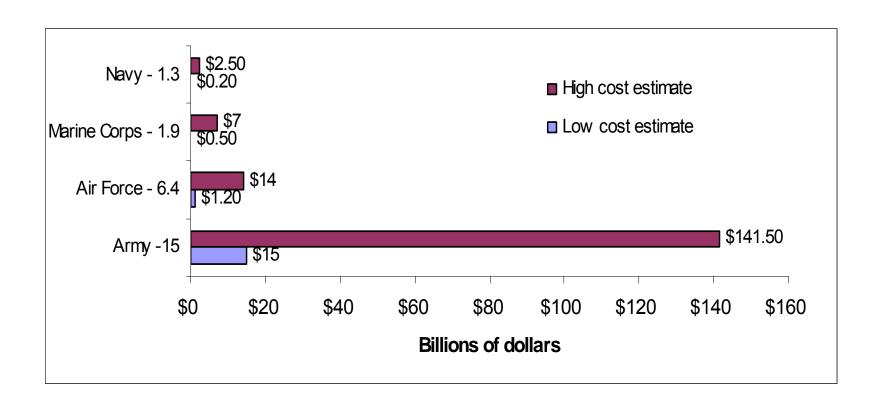
...some management areas not designed to conserve biodiversity, such as military ranges, sometimes do so incidentally and represent some of the last remaining intact habitat in an ecoregion, even though they are not usually included in lists of protected areas. - Ricketts et al. 1999







## **Range Cleanup Estimates**



GAO 2004. Operational Ranges Report, 04-0601





## **Environmental contamination**

- Has affected OPTEMPO
  - Sustainability
  - Off-site migration
  - Remediation
  - Schedule
- Closed ranges
  - Review panels
- Sites include
  - Manufacturing
  - Load/pack plants
  - Ranges
  - OB/OD areas











# **Objectives**

- What ESOH criteria are relevant to understand environmental impacts?
  - Toxicology
    - Occupational exposures (e.g. inhalation, ocular, dermal)
    - Environmental exposures
      - Human health (e.g., oral)
      - Wildlife
  - Exposure
    - Food web modeling
  - Fate and transport
    - Chemical/physical properties
    - Persistence





### **ESOH** Issues

**Exposure** 

- Persistence
  - Fate
- Transport
  - Bioaccumulation/Biomagnification
- Toxicity
  - Humans
  - Wildlife
  - Invertebrates
  - Plants
- What do you need to know and when do you need to know it?
  - Toxicology studies are expensive.
  - Various levels of certainty
  - HTS methods available



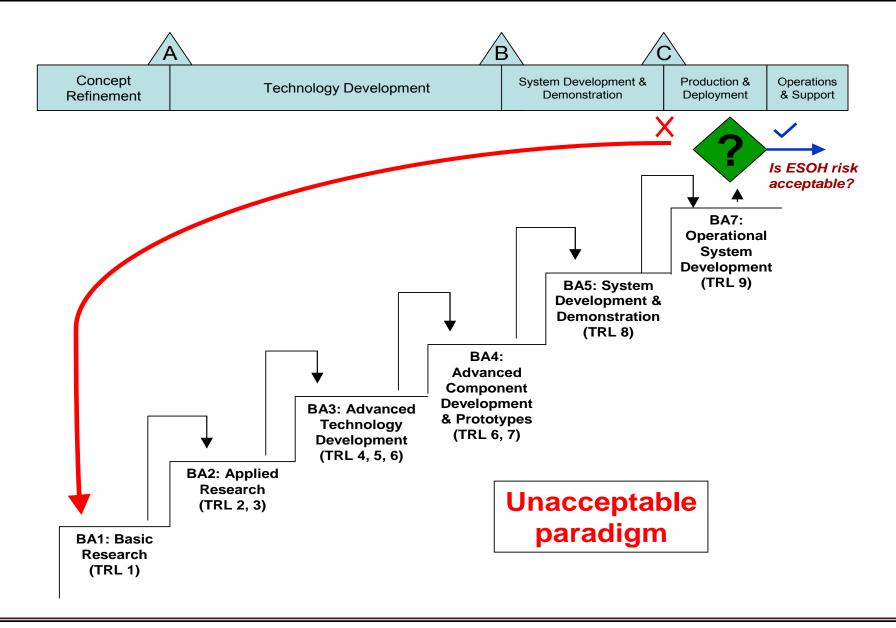


### **Lessons Learned**

- Perchlorate
  - Highly water soluble, weak affinity to organic carbon
  - Low acute toxicity
    - Endocrine disrupting compound
- RDX
  - Not highly water soluble or has a strong affinity to organic carbon
  - High acute toxicity, readily absorbable, convulsions
  - Weak evidence for carcinogenicity







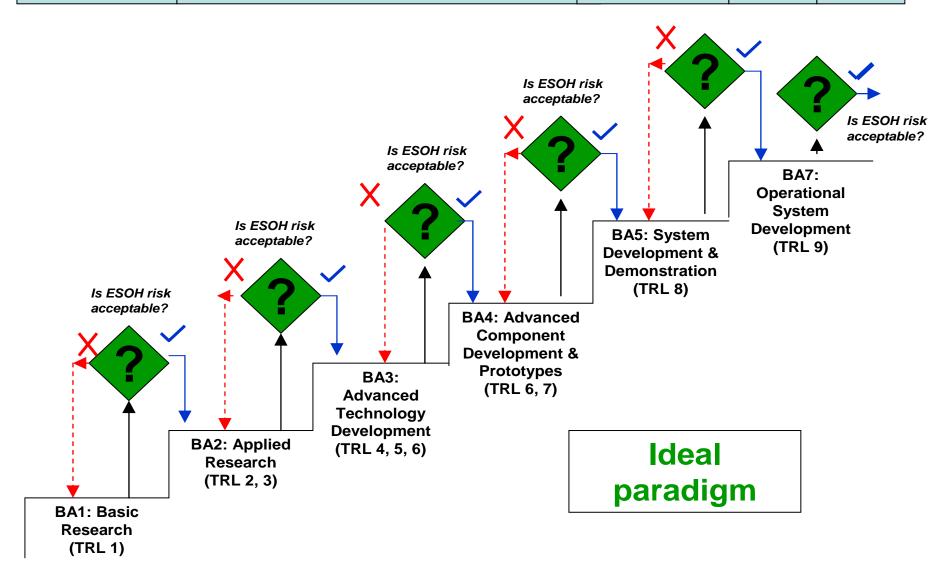
Concept Refinement

**Technology Development** 

System Development & Demonstration

Production & Deployment

Operations & Support







# Phased approach

- ASTM E-2552 Standard Guide for Assessing the Environmental and Human Health Impacts of New Energetic Compounds.
- Models QSARs
- In vitro toxicology
- In vivo toxicology
- Aligned with RDT&E level of effort
- Used in the Ordnance Environmental Program

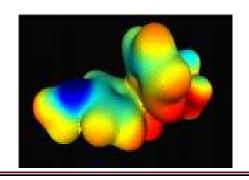






# Levels of Research, Development, Testing and Evaluation

- Conception computer simulation only
- Synthesis labtop operation, small quantities
- Demonstration/Validation refinement of synthesis, stabilization of mixtures, use of COTS.
- Testing System evaluation









## **Stage**

Conception

**Synthesis** 

**Testing** 

Dem/val

**Production** 

Storage & Use

**Demil** 

### **Action**

Computer modeling (QSAR)

Develop empirical chem. prop. data

Conduct toxicity testing
Tier 1

Conduct toxicity testing
Tier 2; Tier 1 Ecotox screening

Tier II Ecotox toxicity testing

Monitoring

Monitoring

### Data req.

Chem/phys. properties Human toxicity estimates

Chem/phys. properties (estimate fate, transport, Bioaccumulation)

Toxicity data, acute In vitro screen

Toxicity data, subchronic

Toxicity data, cancer

Media samples

Media samples

cost

uncertainty





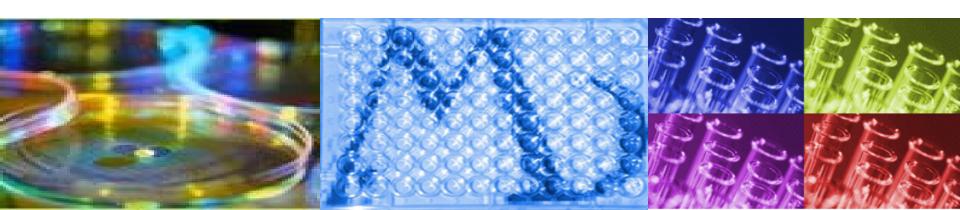
### IN VITRO ASSAYS

### Cell-Based In Vitro

- Primary cell cultures cells & tissues (ex vivo)
- Permanent cell cultures
   human and animal cell lines

### **Useful in RDT&E**

- ► Toxicological screening
- ► Fast, low cost
- Uses small quantities (<1g)</p>
- New tools available
  - Ecotox
  - Cancer
  - Mechanistic

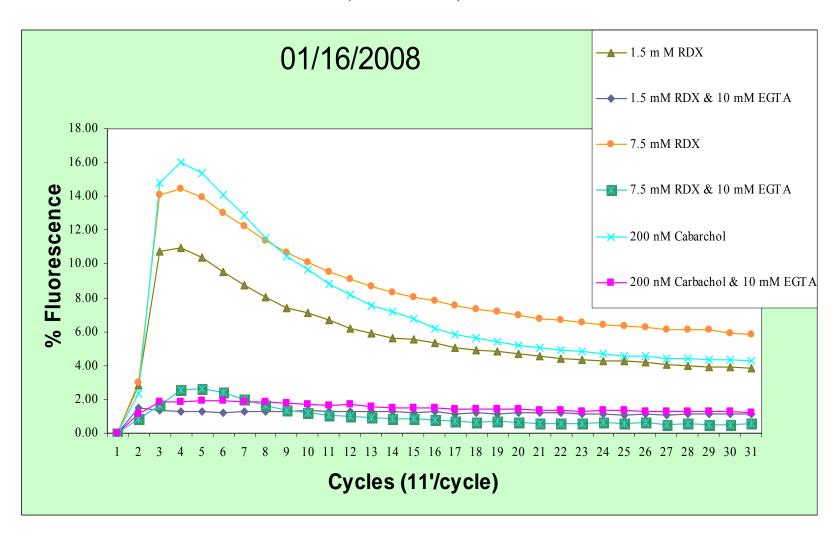








# CELLULAR CALCIUM OF HUMAN NEUROBLASTOMA (SH-SY5Y)







## Criteria

# Toxicology

Human	Eco
Acute – LD50/LC50	Aquatic – LC50
	Invertebrate – LC50
Subchronic	Subchronic
Rat LOAEL	EC20 (growth, repro)
Cancer – in vitro screen;	Amphibian, Avian data*
Rodent bioassay*	

<sup>\*</sup>Data not always present





## **Criteria**

## Chemical/Physical Properties

Criterion	Relevance	Resource affected
Water solubility	Transport	Groundwater
Fat solubility (Log Kow)	Bioaccumulation	Conc. in biota
Vapor pressure	Pathway (inh) Persistence	Occupational vs. environmental exposures
Boiling point/melting point	Pathway (inh) Persistence	Occupational vs. environmental exposures
Henry's Law	Persistence in water	Aquatic organisms
Affinity to carbon (log Koc)	Transport	Groundwater
Friability	Transport	Groundwater

	LOW	MODERATE	HIGH
PERSISTANCE	Readily biodegrades (<28d)	Degradation ½ life: water <40 d soil <120 d	Degradation ½ life: water >40 d soil > 120 d
TRANSPORT	Water sol. < 10 mg/L Log Koc > 2.0	Water sol. 10-1000 mg/L Log Koc 2.0-1.0	Water sol. > 1000 mg/L Log Koc <1.0
BIOACCUMULATION	log Kow <3.0	log Kow 3.0-4.5	log Kow >4.5
TOXICITY	No evidence of carcinogenicity/ mutagenicity; Subchronic LOAEL > 200 mg/kg-d	Mixed evidence for carcinogenicity/ mutagenicity (B2, 2); Subchronic LOAEL 5-200 mg/kg-d	Positive corroborative evidence for carcinogenicity/ mutagenicity; LOAEL < 5 mg/kg-d
ECOTOXICITY	Acute LC(D)50 >1 mg/L or 1500 mg/kg; Subchronic EC50 >100 μg/L or LOAEL >100 mg/kg-d	Acute LC(D)50 1-0.1 mg/L or 1500-150 mg/kg; Subchronic EC50 100-10 μg/L or LOAEL – 10- 100 mg/kg-d	Acute LC(D)50 <100 μg/L or <150 mg/kg; Subchronic LOAEL <10 mg/kg-d





#### Recommended documentation

- Environmental Health Assessments
  - Weapon system specific toxicity profile + fate and transport info.
    - Substance profiles
    - Tables
    - Regulatory values
    - Uncertainty assessment
    - Conclusions
    - Recommendations
  - Conducted consistent with weapon system developers – interactive and iterative process.
  - Technical foundation for PESHE and HHA -TCs





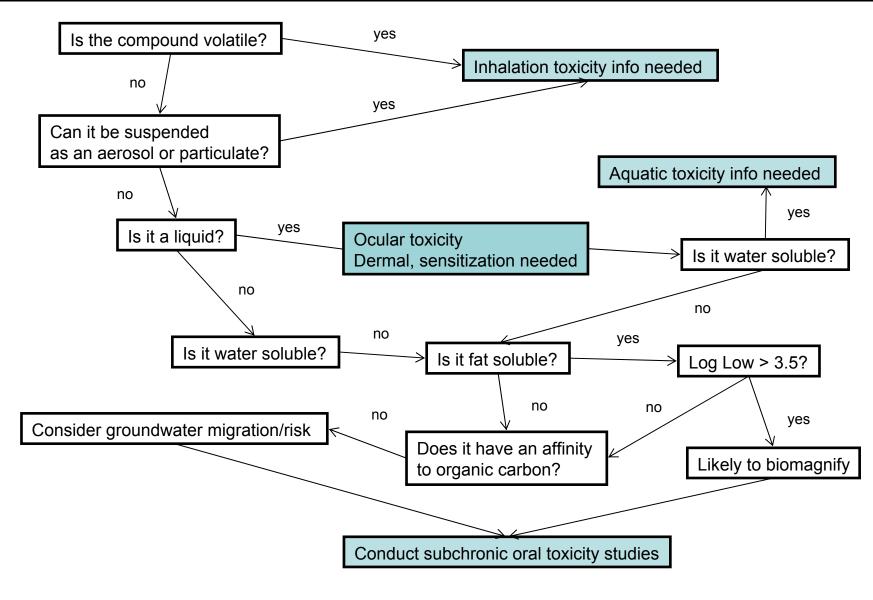
## **ESOH** questions

- Conception
  - Is it readily water soluble? Bioaccumulative? (QSPR)
  - QSARs
    - Reproductive toxicant? MOA?
    - Predicted probability to be carcinogenic
    - Predicted subchronic rat NOAEL
    - Predicted fish LC50, EC50
- Synthesis
  - Is it readily water soluble? Bioaccumulative? (exp. data req.).
  - In vitro/ligand
    - Is it neurotoxic?
    - Aquatic toxicity Vibrio fischeri
    - Acute mammalian toxicity NRU
    - Functional mammalian toxicity Immunotoxicity, mutagenticity, genotoxicity, etc.



### **ESOH flow chart**









### **Lessons Learned**

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#### RDX

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## **Current Projects**

System	Proponent	Stage
Novel RDX replacements	ARL	Conception
Green detonators	ARDEC	Testing
Black smoke	ARDEC	Testing
Red/Violet smoke	ARDEC	Testing
High nitrogen polymers	ARL	Synthesis
M117/M118/M119 simulators	ARDEC	Manufacturing
Hybrid propellants	AMRDEC	Testing
M126A1 Transition	ARDEC	Testing
2.75-in Rocket Propellant transition	AMRDEC	Testing





### **Smokes**

- M18 upgrade
  - Replace violet dyes
  - Solvent Violet 47
- Toxicity test
  - Rat inhalation (LC50)
  - 70% mortality at 2.6 mg/L
- Result
  - Replaced with red and blue dyes with reduced toxicity











## **Nanomaterials**

- Biological properties could differ significantly from those of chemical and biological substances in other physical forms.
- Toxicity influenced by:
  - a) particle size
  - b) particle shape
  - c) surface chemistry (charge)
  - d) presence of other materials
  - e) Aggregation status
  - f) Number of particles
  - Primary particle size





### **Summary**

- Iterative engagement with ESOH professionals is beneficial.
  - RDT&E
  - Acquisition
  - Production
  - Demil
- Data requirements are needed.
  - Question based.
  - Integrate data needs across ESOH
    - Focus on targets
  - Need additional methods to address questions:
    - HTS (in vitro) methods
    - Energetic-specific QSARs
      - Require robust toxicity database





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